

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

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| Applicant's or agent's file reference P205623PCT SMO | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
| International application No. PCT/NL 03/00922 | International filing date (day/month/year) 23.12.2003 | Priority date (day/month/year) 23.12.2002 |
| International Patent Classification (IPC) or both national classification and IPC C12N5/00 | | |
| Applicant FUJI PHOTO FILM B.V. et al. | | |

1. This International preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I Basis of the opinion
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

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| Date of submission of the demand 22.07.2004 | Date of completion of this report 02.03.2005 |
| Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized Officer Grötzinger, T Telephone No. +49 89 2399-7166 |



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/NL 03/00922

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-16 as originally filed

Claims, Numbers

1-11 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

| | | |
|-------------------------------|-------------|------------|
| Novelty (N) | Yes: Claims | 8,11 |
| | No: Claims | 1-7, 9, 10 |
| Inventive step (IS) | Yes: Claims | - |
| | No: Claims | 8, 11 |
| Industrial applicability (IA) | Yes: Claims | 1-11 |
| | No: Claims | - |

2. Citations and explanations

see separate sheet

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Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: WO91/07485
- D2: SIGMA ProductInformation Sheet
- D3: US4,994,388
- D4: WO01/34646

1. Novelty (Article 33(2) PCT)

Claims 1 to 7, 9, and 10 are not novel in accordance with Article 33(2) PCT.

1.1 Claims 1 to 6

Claim 1 relates to a process for preparing coated cell culture microcarriers comprising the use of gelatine "having a molecular weight of about 40 kDa to about 200 kDa". WO91/07485 (D1) discloses a process in which polystyrene beads are coated with gelatin (Type A, 300 Bloom from Sigma) (page 17, last paragraph). It is common general knowledge that gelatin with a gel strength of 300 Bloom corresponds to a protein mixture with an average MW of 50,000 to 100,000 (see, e.g., page 3 of SIGMA ProductInformation Sheet (D2) that can be found under <http://www.sigmaaldrich.com/cgi-bin/hsrun/Distributed/HahtShop/HAHTpage/frmCatalogSearchPost?Brand=SIGMA&ProdNo=G2500>; a copy thereof is enclosed for the Applicant's information). Thus, it appears as if WO91/07485 (D1) discloses a process as claimed in claims 1, 4, and 5.

According to WO91/07485 (D1), a crosslinking agent may be furthermore used to immobilize the cell adhesion proteins onto the beads (page 18, second paragraph). The beads, as mentioned above, are made out of polystyrene which is non-porous (page 9, last sentence) but the use of (porous) dextran is also anticipated (e.g., page 9, penultimate sentence, or page 11, bottom of first paragraph). Hence, WO91/07485 (D1) is also novelty-destroying for claims 2, 3, and 6.

1.2 Claims 7, 9, and 10

Regarding claims 7, 9, and 10, it cannot be excluded at the moment that the gelatin used

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in WO91/07485 (D1) inherently also shows the features disclosed in claims 7, 9, and 10. Thus, WO91/07485 (D1) is also detrimental for novelty of those claims.

1.3 Claims 8 and 11 appear to be novel over the cited prior art.

2. Inventive Step (Article 33(3) PCT)

Claims 8 and 11 are not inventive as required by Article 33(3) PCT.

2.1 Claim 8

Closest prior art: US4,994,388 (D3) may be regarded as closest prior art. This document discloses a process for preparing microcarriers coated with collagen, wherein the collagen is obtained from natural sources (column 3, lines 52 to 56, and column 6, lines 28 to 33).

Technical problem: According to the Applicant, it was the object of the invention to provide processes for coating microcarriers with gelatine such that the particles do not clump afterwards in cell cultures (page 3, third paragraph). This is in agreement with the technical problem that can be seen in view of the closest prior art US4,994,388 (D3), namely the provision of processes yielding particles of superior quality.

Solution: According to the application, this problem is solved by using recombinant gelatin instead of gelatin from natural sources.

This solution, however, cannot be regarded as involving an inventive step in light of WO01/34646 (D4). This document discloses recombinant gelatin and proposes to use the same for coating purposes (page 59, lines 25 to 28; page 71, lines 33 to 39; page 72, lines 12 to 16). Moreover, it is discussed in detail which advantages the recombinant gelatin offers. In particular, it is said that gelatins with specific physico-chemical characteristics can be produced. These include the isoelectric profile, a specific molecular weight or specific ranges thereof, and the degree of hydroxylation, (page 28, lines 31 to 36; page 31, lines 27 to 39; page 32, lines 5 to 11; page 34, lines 21 to 24). Thus, it appears as if claim 7 represents an obvious solution at which the person skilled in the art would arrive without further ado when trying to amend production processes in order to improve the features of microcarriers.

2.2 Claim 11

As regards claim 11, it appears as if the size of the beads indicated in the claim is a

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standard range that cannot establish inventive step (see US4,994,388 (D3), column 3, lines 57 to 60).